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The effectiveness and efficacy of the combination of pharmacotherapy with the two new recovery-oriented programs, RECOVERYTRSGR for patients with treatment- resistant schizophrenia and RECOVERYTRSBDGR for patients with treatment- resistant bipolar disorder.

Dr. phil., Dipl.-Psych., Stavroula Rakitzi

Clinical psychologist and cognitive behavioral psychotherapist

Private practice

ILISION 34 15771 Athens Greece

2111180571

6989766935

Stavroula@Rakitzi.onmicrosoft.com

Description linkedin Stavroula Rakitzi

ORCID: http://0000-0002-5231-6619

Polyxeni Georgila, M. D. Psychiatrist and cognitive behavioral psychotherapist

Private practice

ILISION 34 15771 Athens Greece

6932905259

polyxenigeorgila@gmail.com

Description linkedin Polyxeni Georgila

ORCID: http://0000-0003-3137-506X

Chronic mental health disorders present a huge burden for the patients and their families. Long-term pharmacotherapy and long-term recovery-oriented psychotherapy are important treatments to cope with this burden.

Schizophrenia and bipolar disorders present the most difficult chronic mental health disorders. Both are associated with high suicidal risk, cognitive impairment, many dropouts, bad adherence to treatments, and many hospitalizations. Treatment resistant schizophrenia and treatment resistant bipolar disorder are two subcategories of these mental health disorders, which are linked to higher suicidal risk, exacerbated cognitive impairment and numerous hospitalizations.

Treatment-resistant means that patients do not respond favorably to most of the medications, and certain combinations of agents work well for these patient groups. The sooner schizophrenia and bipolar disorder are diagnosed as treatment-resistant, the better for the patient, the psychiatrist and the cognitive behavioral psychotherapist.

RECOVERYTRSGR (Rakitzi & Georgila, 2024) and RECOVERYTRSBDGR (Rakitzi & Georgila, 2024b) are two newly developed recovery-oriented programs for patients with treatment-resistant schizophrenia and patients with treatment-resistant bipolar disorder, which were developed by us. These programs are the consequence of our clinical experience with treatment-resistant patients with schizophrenia and bipolar disorder and the difficulties of the Greek Health System (private and public sector) with these two disorders. These recovery-oriented programs aim to help patients to reintegrate into society from the recovery perspective, to gain more awareness towards the disorder, to be more responsible towards their problems, and to be more assertive towards their own human rights.

RECOVERYTRSGR for patients with treatment-resistant schizophrenia contains 190 therapeutic sessions. The introductory phase contains 20 sessions. The second phase

contains 160 sessions with individual and group cognitive behavioral psychotherapy and rehabilitation. The third phase contains 8 sessions (an epilogue), and finally, two monthly follow-ups provided at the end.

Selection criteria: *Inclusion criteria:* age 18-65, IQ ≥ 80, diagnosis TRS. *Exclusion criteria:* Substance abuse and head injury. If substance abuse is successfully treated, the participant will be accepted into our program.

Reliable and valid tests are going to be administered before the therapy, after the therapy and in a follow-up after 6 months after therapy.

Aster et al. (2006) should be used before treatment to show the burden of cognitive dysfunction and intellectual ability, and it is repeatable after one year. An intelligence quotient (IQ) ≥ 80 is a necessary condition to participate in our recovery model for TRS.

The Matrics Consensus Cognitive Battery (MCCB) (Nuechterlein & Green, 2006) for cognitive functions, the Greek verbal memory test for the evaluation of the verbal memory (Kosmidou & Vlahou, 2010), the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987; Lykouras et al., 2005), WHODAS 2 0 (Koumpouros et al., 2018; WHO, 2001) for disability and functional capacity, the Recovery Assessment Scale-Domains and Stages (RAS-DS) (Hancock et al., 2019, 2023) for the evaluation of the recovery process and clinical global impression scale (CGI) for the evaluation of the global functioning (Busner & Targum, 2007; Guy, 1976) are going to be administered before the therapy, after the therapy and in a follow-up after 6 months.

RECOVERYTRSBDGR contains 140 sessions. The introductory phase contains 20 sessions. The second phase contains 108 sessions with individual and group

cognitive behavioral psychotherapy and rehabilitation. The third phase contains 8 sessions (an epilogue), and finally, four monthly follow-ups provided at the end.

An intelligence quotient (IQ) ≥ 80 is a necessary condition to participate in our recovery model for TRSBD. Selection criteria: *inclusion criteria:* age 18-65, IQ ≥ 80, diagnosis

TRSBD. *Exclusion criteria:* Substance abuse and head injuries. If substance abuse is successfully treated, the participant will be acknowledged into our program.

WAIS (Aster et al., 2006) should be used before treatment to show the burden of cognitive dysfunction and intellectual ability, and it is repeatable after one year. The symptom checklist 90-R (Donias et al., 1991), the Altman self-rating Mania Scale (Altman et al., 1997) (Greek Version), the Young Mania Rating Scale (Young et al., 1978), the Symptoms Rating Scale for Depression and Anxiety (SRSDSA) (Bech, 1993; Fountoulakis, 2003), the Hamilton Depression Scale (HAM-D) (Hamilton, 1960) (the Greek version), the Montgomery and Asperg Depression Rating Scale (MADRS) (Montgomery & Asperg, 1979; Williams & Kobak, 2008) (the Greek version) and the psychotic symptom rating scales (PSYRATS) (Haddock, 1999) can also be used.

WHODAS 2. 0 (Koumpouros et al., 2018; WHO, 2001) for disability and functional capacity, the Recovery Assessment Scale-Domains and Stages (RAS-DS) for the evaluation of the recovery process (Hancock et al., 2019, 2023) and clinical global impression scale (CGI) for the evaluation of the global functioning (Busner & Targum, 2007; Guy, 1976) offer valid and reliable tests. All the above-mentioned tests are going to be administered before the therapy, after the therapy and in a follow-up after 6 months.

Our research project aims to evaluate the efficacy and effectiveness of the combination of pharmacotherapy with these two programs. The project will begin in May 2025 and finish in December 2027.

RECOVERYTRSGR will be compared to treatment as usual (TAU) and RECOVERYTRSBDGR will be compared also to TAU. TAU means that patients with treatment-resistant schizophrenia will participate in 190 sessions-2 times monthly

psychiatric treatment and individual psychotherapy (psychoeducation, cognitive behavioral psychotherapy and psychoeducation to family, social skills training). TAU by treatment resistant bipolar disorder, means that patients will participate in 140 session-2 times monthly psychiatric treatment and individual psychotherapy (psychoeducation, cognitive behavioral psychotherapy, psychoeducation to family, social skills training).

Tests will be given before the therapy, after the therapy and in a follow-up after 6 months.

Study population

The outpatients with treatment resistant schizophrenia and treatment resistant bipolar disorder will be recruited by Dr. Stavroula Rakitzi, clinical psychologist and cognitive behavioral psychotherapist and Dr. Polyxeni Georgila, psychiatrist and cognitive behavioral psychotherapist from their own private practice.

Compliance with ethical standards

Prior to the study's inclusion, the patients will read and sign written informed consent for their involvement in this research project. Information that could reveal the patients' identities was left out. The authors adhere to the APA ethical standards.

Scientists who treat patients in private practices are not prohibited by Greek authorities from undertaking research projects. Private sector scientists' research efforts are not reviewed by an ethical body.

Statistical analysis

A GLM and regression analysis should be performed to see if the therapy groups RECOVERYTRSGR and RECOVERYTRSBDGR are more effective and efficacious

in comparison to TAU and specifically which variables can explain better this efficacy and effectiveness. Effect sizes will also be computed.

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